



Substitute Sequence Listing 08702-0100.txt
SEQUENCE LISTING

<110> Wyeth
Wolfman, Neil

<120> MODIFIED AND STABILIZED GDF PROPEPTIDES AND USES THEREOF

<130> 08702.0100-00000

<150> 10/071,499

<151> 2002-02-08

<150> 60/257,509

<151> 2001-02-08

MAR 01 2004

<160> 23

<170> PatentIn version 3.1

<210> 1

<211> 375

<212> PRT

<213> Homo sapiens

<400> 1

Met Gln Lys Leu Gln Leu Cys Val Tyr Ile Tyr Leu Phe Met Leu Ile
1 5 10 15

Val Ala Gly Pro Val Asp Leu Asn Glu Asn Ser Glu Gln Lys Glu Asn
20 25 30

Val Glu Lys Glu Gly Leu Cys Asn Ala Cys Thr Trp Arg Gln Asn Thr
35 40 45

Lys Ser Ser Arg Ile Glu Ala Ile Lys Ile Gln Ile Leu Ser Lys Leu
50 55 60

Arg Leu Glu Thr Ala Pro Asn Ile Ser Lys Asp Val Ile Arg Gln Leu
65 70 75 80

Leu Pro Lys Ala Pro Pro Leu Arg Glu Leu Ile Asp Gln Tyr Asp Val
85 90 95

Gln Arg Asp Asp Ser Ser Asp Gly Ser Leu Glu Asp Asp Asp Tyr His
100 105 110

Ala Thr Thr Glu Thr Ile Ile Thr Met Pro Thr Glu Ser Asp Phe Leu
115 120 125

Met Gln Val Asp Gly Lys Pro Lys Cys Cys Phe Phe Lys Phe Ser Ser
130 135 140

Lys Ile Gln Tyr Asn Lys Val Val Lys Ala Gln Leu Trp Ile Tyr Leu
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145          150          155          160
Arg Pro Val Glu Thr Pro Thr Thr Val Phe Val Gln Ile Leu Arg Leu
          165          170          175
Ile Lys Pro Met Lys Asp Gly Thr Arg Tyr Thr Gly Ile Arg Ser Leu
          180          185          190
Lys Leu Asp Met Asn Pro Gly Thr Gly Ile Trp Gln Ser Ile Asp Val
          195          200          205
Lys Thr Val Leu Gln Asn Trp Leu Lys Gln Pro Glu Ser Asn Leu Gly
          210          215          220
Ile Glu Ile Lys Ala Leu Asp Glu Asn Gly His Asp Leu Ala Val Thr
          225          230          235
Phe Pro Gly Pro Gly Glu Asp Gly Leu Asn Pro Phe Leu Glu Val Lys
          245          250          255
Val Thr Asp Thr Pro Lys Arg Ser Arg Arg Asp Phe Gly Leu Asp Cys
          260          265          270
Asp Glu His Ser Thr Glu Ser Arg Cys Cys Arg Tyr Pro Leu Thr Val
          275          280          285
Asp Phe Glu Ala Phe Gly Trp Asp Trp Ile Ile Ala Pro Lys Arg Tyr
          290          295          300
Lys Ala Asn Tyr Cys Ser Gly Glu Cys Glu Phe Val Phe Leu Gln Lys
          305          310          315
Tyr Pro His Thr His Leu Val His Gln Ala Asn Pro Arg Gly Ser Ala
          325          330          335
Gly Pro Cys Cys Thr Pro Thr Lys Met Ser Pro Ile Asn Met Leu Tyr
          340          345          350
Phe Asn Gly Lys Glu Gln Ile Ile Tyr Gly Lys Ile Pro Ala Met Val
          355          360          365
Val Asp Arg Cys Gly Cys Ser
          370          375

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<210> 2
<211> 1125
<212> DNA
<213> Homo sapiens

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<400> 2
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gtggatctaa atgagaacag tgagcaaaaa gaaaatgtgg aaaaagaggg gctgtgtaat 120
gcatgtactt ggagacaaaa cactaaatct tcaagaatag aagccattaa gatacaaatc 180
ctcagtaaac ttcgtctgga aacagctcct aacatcagca aagatgttat aagacaactt 240
ttacccaaag ctctccact ccgggaactg attgatcagt atgatgtcca gagggatgac 300
agcagcgatg gctctttgga agatgacgat tatcacgcta caacggaaac aatcattacc 360
atgcctacag agtctgattt tctaatacaa gtggatggaa aaccctaatg ttgcttcttt 420
aaatttagct ctaaaataca atacaataaa gtagtaaagg cccaactatg gatataattg 480
agaccgcgtg agactcctac aacagtgttt gtgcaaatcc tgagactcat caaacctatg 540
aaagacggta caagggtatac tggaatccga tctctgaaac ttgacatgaa cccaggcact 600
ggtatttggc agagcattga tgtgaagaca gtgttgcaaa attggctcaa acaacctgaa 660
tccaacttag gcattgaaat aaaagcttta gatgagaatg gtcatgatct tgctgtaacc 720
ttcccaggac caggagaaga tgggctgaat ccgttttttag aggtcaagggt aacagacaca 780
ccaaaaagat ccagaaggga ttttggtctt gactgtgatg agcactcaac agaatacga 840
tgctgtcggt accctctaac tgtggatttt gaagcttttg gatgggattg gattatcgct 900
cctaaaagat ataaggccaa ttactgctct ggagagtgtg aatttgtatt tttaaaaaa 960
tatcctcata ctcatctggt acaccaagca aaccccagag gttcagcagg cccttgctgt 1020
actcccacaa agatgtctcc aattaatatg ctatatttta atggcaaaga acaaataata 1080
tatgggaaaa ttccagcgat ggtagtagac cgctgtgggt gctca 1125

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<210> 3
<211> 109
<212> PRT
<213> Homo sapiens

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<400> 3
Asp Phe Gly Leu Asp Cys Asp Glu His Ser Thr Glu Ser Arg Cys Cys
1 5 10 15

Arg Tyr Pro Leu Thr Val Asp Phe Glu Ala Phe Gly Trp Asp Trp Ile
20 25 30

Ile Ala Pro Lys Arg Tyr Lys Ala Asn Tyr Cys Ser Gly Glu Cys Glu
35 40 45

Phe Val Phe Leu Gln Lys Tyr Pro His Thr His Leu Val His Gln Ala
50 55 60

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Asn Pro Arg Gly Ser Ala Gly Pro Cys Cys Thr Pro Thr Lys Met Ser
65 70 75 80

Pro Ile Asn Met Leu Tyr Phe Asn Gly Lys Glu Gln Ile Ile Tyr Gly
85 90 95

Lys Ile Pro Ala Met Val Val Asp Arg Cys Gly Cys Ser
100 105

<210> 4
<211> 327
<212> DNA
<213> Homo sapiens

<400> 4
gattttggtc ttgactgtga tgagcactca acagaatcac gatgctgtcg ttaccctcta 60
actgtggatt ttgaagcttt tggatgggat tggattatcg ctctaaaag atataaggcc 120
aattactgct ctggagagtg tgaatttgta tttttacaaa aatatacctca tactcatctg 180
gtacaccaag caaacccag aggttcagca ggccttgct gtactccac aaagatgtct 240
ccaattaata tgctatattt taatggcaaa gaacaaataa tatatgggaa aattccagcg 300
atggtagtag accgctgtgg gtgctca 327

<210> 5
<211> 243
<212> PRT
<213> Homo sapiens

<400> 5
Asn Glu Asn Ser Glu Gln Lys Glu Asn Val Glu Lys Glu Gly Leu Cys
1 5 10 15
Asn Ala Cys Thr Trp Arg Gln Asn Thr Lys Ser Ser Arg Ile Glu Ala
20 25 30
Ile Lys Ile Gln Ile Leu Ser Lys Leu Arg Leu Glu Thr Ala Pro Asn
35 40 45
Ile Ser Lys Asp Val Ile Arg Gln Leu Leu Pro Lys Ala Pro Pro Leu
50 55 60
Arg Glu Leu Ile Asp Gln Tyr Asp Val Gln Arg Asp Asp Ser Ser Asp
65 70 75 80
Gly Ser Leu Glu Asp Asp Asp Tyr His Ala Thr Thr Glu Thr Ile Ile
85 90 95

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Thr Met Pro Thr Glu Ser Asp Phe Leu Met Gln Val Asp Gly Lys Pro
100 105 110

Lys Cys Cys Phe Phe Lys Phe Ser Ser Lys Ile Gln Tyr Asn Lys Val
115 120 125

Val Lys Ala Gln Leu Trp Ile Tyr Leu Arg Pro Val Glu Thr Pro Thr
130 135 140

Thr Val Phe Val Gln Ile Leu Arg Leu Ile Lys Pro Met Lys Asp Gly
145 150 155 160

Thr Arg Tyr Thr Gly Ile Arg Ser Leu Lys Leu Asp Met Asn Pro Gly
165 170 175

Thr Gly Ile Trp Gln Ser Ile Asp Val Lys Thr Val Leu Gln Asn Trp
180 185 190

Leu Lys Gln Pro Glu Ser Asn Leu Gly Ile Glu Ile Lys Ala Leu Asp
195 200 205

Glu Asn Gly His Asp Leu Ala Val Thr Phe Pro Gly Pro Gly Glu Asp
210 215 220

Gly Leu Asn Pro Phe Leu Glu Val Lys Val Thr Asp Thr Pro Lys Arg
225 230 235 240

Ser Arg Arg

<210> 6
<211> 729
<212> DNA
<213> Homo sapiens

<400> 6
aatgagaaca gtagcaaaa agaaaatgtg gaaaaagagg ggctgtgtaa tgcattgtact 60
tggagacaaa aactaaatc ttcaagaata gaagccatta agatacaaat cctcagtaaa 120
cttcgtctgg aaacagctcc taacatcagc aaagatgtta taagacaact ttaccctaaa 180
gctcctccac tccgggaact gattgatcag tatgatgtcc agagggatga cagcagcgat 240
ggctcttttg aagatgacga ttatcacgct acaacggaaa caatcattac catgcctaca 300
gagtctgatt ttctaatagc agtggatgga aaacccaaat gttgcttctt taaatttagc 360
tctaaaatac aatacaataa agtagtaaag gcccaactat ggatatattt gagaccgctc 420
gagactccta caacagtgtt tgtgcaaata ctgagactca tcaaacttat gaaagacggt 480
acaaggtata ctggaatccg atctctgaaa cttgacatga acccaggcac tggattttgg 540

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cagagcattg atgtgaagac agtgttgcaa aattggctca aacaacctga atccaactta 600
 ggcattgaaa taaaagcttt agatgagaat ggtcatgata ttgctgtaac cttcccagga 660
 ccaggagaag atgggctgaa tccgttttta gaggtcaagg taacagacac accaaaaaga 720
 tccagaagg 729

<210> 7
 <211> 407
 <212> PRT
 <213> Homo sapiens

<400> 7

Met Val Leu Ala Ala Pro Leu Leu Leu Gly Phe Leu Leu Leu Ala Leu
 1 5 10 15

Glu Leu Arg Pro Arg Gly Glu Ala Ala Glu Gly Pro Ala Ala Ala Ala
 20 25 30

Ala Ala Ala Ala Ala Ala Ala Ala Ala Gly Val Gly Gly Glu Arg Ser
 35 40 45

Ser Arg Pro Ala Pro Ser Val Ala Pro Glu Pro Asp Gly Cys Pro Val
 50 55 60

Cys Val Trp Arg Gln His Ser Arg Glu Leu Arg Leu Glu Ser Ile Lys
 65 70 75 80

Ser Gln Ile Leu Ser Lys Leu Arg Leu Lys Glu Ala Pro Asn Ile Ser
 85 90 95

Arg Glu Val Val Lys Gln Leu Leu Pro Lys Ala Pro Pro Leu Gln Gln
 100 105 110

Ile Leu Asp Leu His Asp Phe Gln Gly Asp Ala Leu Gln Pro Glu Asp
 115 120 125

Phe Leu Glu Glu Asp Glu Tyr His Ala Thr Thr Glu Thr Val Ile Ser
 130 135 140

Met Ala Gln Glu Thr Asp Pro Ala Val Gln Thr Asp Gly Ser Pro Leu
 145 150 155 160

Cys Cys His Phe His Phe Ser Pro Lys Val Met Phe Thr Lys Val Leu
 165 170 175

Lys Ala Gln Leu Trp Val Tyr Leu Arg Pro Val Pro Arg Pro Ala Thr
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180

185

190

Val Tyr Leu Gln Ile Leu Arg Leu Lys Pro Leu Thr Gly Glu Gly Thr
195 200 205

Ala Gly Gly Gly Gly Gly Gly Arg Arg His Ile Arg Ile Arg Ser Leu
210 215 220

Lys Ile Glu Leu His Ser Arg Ser Gly His Trp Gln Ser Ile Asp Phe
225 230 235 240

Lys Gln Val Leu His Ser Trp Phe Arg Gln Pro Gln Ser Asn Trp Gly
245 250 255

Ile Glu Ile Asn Ala Phe Asp Pro Ser Gly Thr Asp Leu Ala Val Thr
260 265 270

Ser Leu Gly Pro Gly Ala Glu Gly Leu His Pro Phe Met Glu Leu Arg
275 280 285

Val Leu Glu Asn Thr Lys Arg Ser Arg Arg Asn Leu Gly Leu Asp Cys
290 295 300

Asp Glu His Ser Ser Glu Ser Arg Cys Cys Arg Tyr Pro Leu Thr Val
305 310 315 320

Asp Phe Glu Ala Phe Gly Trp Asp Trp Ile Ile Ala Pro Lys Arg Tyr
325 330 335

Lys Ala Asn Tyr Cys Ser Gly Gln Cys Glu Tyr Met Phe Met Gln Lys
340 345 350

Tyr Pro His Thr His Leu Val Gln Gln Ala Asn Pro Arg Gly Ser Ala
355 360 365

Gly Pro Cys Cys Thr Pro Thr Lys Met Ser Pro Ile Asn Met Leu Tyr
370 375 380

Phe Asn Asp Lys Gln Gln Ile Ile Tyr Gly Lys Ile Pro Gly Met Val
385 390 395 400

Val Asp Arg Cys Gly Cys Ser
405

<210> 8
<211> 1221
<212> DNA
<213> Homo sapiens

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<400> 8
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gcgggggtcg ggggggagcg ctccagccgg ccagccccgt ccgtggcgcc cgagccggac 180
ggctgccccg tgtgcgtttg gcggcagcac agccgcgagc tgcgcctaga gagcatcaag 240
tcgcagatct tgagcaaaact gcggctcaag gaggcgccca acatcagccg cgaggtggtg 300
aagcagctgc tgcccaaggc gccgccgctg cagcagatcc tggacctaca cgacttccag 360
ggcgacgcgc tcagcccga ggacttcctg gaggaggacg agtaccacgc caccaccgag 420
accgtcatta gcatggccca ggagacggac ccagcagtac agacagatgg cagccctctc 480
tgctgccatt ttacttcag cccaagggtg atgttcacaa aggtactgaa ggcccagctg 540
tggggtgtacc tacggcctgt accccgcccc gccacagtct acctgcagat cttgctgacta 600
aaaccctaa ctggggaagg gaccgcaggg ggagggggcg gaggccggcg tcacatccgt 660
atccgctcac tgaagattga gctgcactca cgctcaggcc attggcagag catcgacttc 720
aagcaagtgc tacacagctg gttccgccag ccacagagca actggggcat cgagatcaac 780
gcctttgatc ccagtggcac agacctggct gtcacctccc tggggccggg agccgagggg 840
ctgcatccat tcatggagct tcgagtccta gagaacacaa aacgttcccg gcggaacctg 900
ggctctggact gcgacgagca ctcaagcgag tcccgtgct gccgatatcc cctcacagtg 960
gactttgagg ctttcggctg ggactggatc atcgcaccta agcgctacaa ggccaactac 1020
tgctccggcc agtgcgagta catgttcatg caaaaatatc cgcataccca tttggtgcag 1080
caggccaatc caagaggctc tgctgggccc tgttgtagcc ccaccaagat gtccccaatc 1140
aacatgctct acttcaatga caagcagcag attatctacg gcaagatccc tggcatgggtg 1200
gtggatcgct gtggctgctc t 1221

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<210> 9
<211> 109
<212> PRT
<213> Homo sapiens

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<400> 9
Asn Leu Gly Leu Asp Cys Asp Glu His Ser Ser Glu Ser Arg Cys Cys
1          5          10          15

Arg Tyr Pro Leu Thr Val Asp Phe Glu Ala Phe Gly Trp Asp Trp Ile
          20          25          30

Ile Ala Pro Lys Arg Tyr Lys Ala Asn Tyr Cys Ser Gly Gln Cys Glu
          35          40          45

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Tyr Met Phe Met Gln Lys Tyr Pro His Thr His Leu Val Gln Gln Ala
50 55 60

Asn Pro Arg Gly Ser Ala Gly Pro Cys Cys Thr Pro Thr Lys Met Ser
65 70 75 80

Pro Ile Asn Met Leu Tyr Phe Asn Asp Lys Gln Gln Ile Ile Tyr Gly
85 90 95

Lys Ile Pro Gly Met Val Val Asp Arg Cys Gly Cys Ser
100 105

<210> 10
<211> 327
<212> DNA
<213> Homo sapiens

<400> 10
aacctggggtc tggactgcga cgagcactca agcgagtccc gctgctgccg atatcccctc 60
acagtggact ttgaggcttt cggctgggac tggatcatcg cacctaagcg ctacaaggcc 120
aactactgct cgggccagtg cgagtacatg ttcatgcaaa aatatccgca taccatttg 180
gtgcagcagg ccaatccaag aggctctgct gggccctggt gtacccccac caagatgtcc 240
ccaatcaaca tgctctactt caatgacaag cagcagatta tctacggcaa gatccctggc 300
atggtggtgg atcgctgtgg ctgctct 327

<210> 11
<211> 274
<212> PRT
<213> Homo sapiens

<400> 11
Ala Glu Gly Pro Ala Ala Ala Ala Ala Ala Ala Ala Ala Ala Ala Ala
1 5 10 15
Ala Gly Val Gly Gly Glu Arg Ser Ser Arg Pro Ala Pro Ser Val Ala
20 25 30
Pro Glu Pro Asp Gly Cys Pro Val Cys Val Trp Arg Gln His Ser Arg
35 40 45
Glu Leu Arg Leu Glu Ser Ile Lys Ser Gln Ile Leu Ser Lys Leu Arg
50 55 60
Leu Lys Glu Ala Pro Asn Ile Ser Arg Glu Val Val Lys Gln Leu Leu
65 70 75 80

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Pro Lys Ala Pro Pro Leu Gln Gln Ile Leu Asp Leu His Asp Phe Gln
85 90 95

Gly Asp Ala Leu Gln Pro Glu Asp Phe Leu Glu Glu Asp Glu Tyr His
100 105 110

Ala Thr Thr Glu Thr Val Ile Ser Met Ala Gln Glu Thr Asp Pro Ala
115 120 125

Val Gln Thr Asp Gly Ser Pro Leu Cys Cys His Phe His Phe Ser Pro
130 135 140

Lys Val Met Phe Thr Lys Val Leu Lys Ala Gln Leu Trp Val Tyr Leu
145 150 155 160

Arg Pro Val Pro Arg Pro Ala Thr Val Tyr Leu Gln Ile Leu Arg Leu
165 170 175

Lys Pro Leu Thr Gly Glu Gly Thr Ala Gly Gly Gly Gly Gly Gly Arg
180 185 190

Arg His Ile Arg Ile Arg Ser Leu Lys Ile Glu Leu His Ser Arg Ser
195 200 205

Gly His Trp Gln Ser Ile Asp Phe Lys Gln Val Leu His Ser Trp Phe
210 215 220

Arg Gln Pro Gln Ser Asn Trp Gly Ile Glu Ile Asn Ala Phe Asp Pro
225 230 235 240

Ser Gly Thr Asp Leu Ala Val Thr Ser Leu Gly Pro Gly Ala Glu Gly
245 250 255

Leu His Pro Phe Met Glu Leu Arg Val Leu Glu Asn Thr Lys Arg Ser
260 265 270

Arg Arg

<210> 12
<211> 822
<212> DNA
<213> Homo sapiens

<400> 12
gccgagggcc ccgcggcggc ggcggcggcg gcggcggcgg cggcagcggc gggggtcggg 60
ggggagcgct ccagccggcc agccccgtcc gtggcgcccc agccggacgg ctgccccgtg 120

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cccaaggcgc	cgccgctgca	gcagatcctg	gacctacacg	acttccaggg	cgacgcgctg	300
cagcccgagg	acttcctgga	ggaggacgag	taccacgcca	ccaccgagac	cgtcattagc	360
atggcccagg	agacggaccc	agcagtacag	acagatggca	gccctctctg	ctgccatttt	420
cacttcagcc	ccaaggatgat	gttcacaaag	gtactgaagg	cccagctgtg	ggtgtaccta	480
cggcctgtac	cccgcccagc	cacagtctac	ctgcagatct	tgcgactaaa	accctaact	540
ggggaagggg	ccgcaggggg	agggggcgga	ggccggcgtc	acatccgtat	ccgctcactg	600
aagattgagc	tgcactcacg	ctcaggccat	tggcagagca	tcgacttcaa	gcaagtgcta	660
cacagctggt	tccgccagcc	acagagcaac	tggggcatcg	agatcaacgc	ctttgatccc	720
agtggcacag	acctggctgt	cacctccctg	gggccgggag	ccgaggggct	gcatccattc	780
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<210> 13
<211> 23
<212> PRT
<213> Homo sapiens
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<400> 13

Met Gln Lys Leu Gln Leu Cys Val Tyr Ile Tyr Leu Phe Met Leu Ile
1 5 10 15

Val Ala Gly Pro Val Asp Leu
20

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<210> 14
<211> 24
<212> PRT
<213> Homo sapiens
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<400> 14

Met Val Leu Ala Ala Pro Leu Leu Leu Gly Phe Leu Leu Leu Ala Leu
1 5 10 15

Glu Leu Arg Pro Arg Gly Glu Ala
20

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<210> 15
<211> 232
<212> PRT
<213> Homo sapiens
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<400> 15

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Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
1 5 10 15

Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
20 25 30

Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
35 40 45

Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
50 55 60

Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
65 70 75 80

Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
85 90 95

Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
100 105 110

Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
115 120 125

Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr
130 135 140

Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
145 150 155 160

Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
165 170 175

Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
180 185 190

Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
195 200 205

Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
210 215 220

Ser Leu Ser Leu Ser Pro Gly Lys
225 230

<210> 16
<211> 227
<212> PRT

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<213> Homo sapiens

<400> 16

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Leu Gly
1 5 10 15

Ala Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
20 25 30

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
35 40 45

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
50 55 60

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
65 70 75 80

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
85 90 95

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
100 105 110

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
115 120 125

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
130 135 140

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
145 150 155 160

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
165 170 175

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
180 185 190

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
195 200 205

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
210 215 220

Pro Gly Lys
225

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<210> 17
 <211> 4
 <212> PRT
 <213> Homo sapiens

<400> 17

Gly Ser Gly Ser
 1

<210> 18
 <211> 4
 <212> PRT
 <213> Human

<400> 18

Arg Ser Arg Arg
 1

<210> 19
 <211> 7
 <212> PRT
 <213> Human

<400> 19

Ala Glu Gly Pro Ala Ala Ala
 1 5

<210> 20
 <211> 498
 <212> PRT
 <213> chimera

<400> 20

Met Met Gln Lys Leu Gln Met Tyr Val Tyr Ile Tyr Leu Phe Met Leu
 1 5 10 15

Ile Ala Ala Gly Pro Val Asp Leu Asn Glu Gly Ser Glu Arg Glu Glu
 20 25 30

Asn Val Glu Lys Glu Gly Leu Cys Asn Ala Cys Ala Trp Arg Gln Asn
 35 40 45

Thr Arg Tyr Ser Arg Ile Glu Ala Ile Lys Ile Gln Ile Leu Ser Lys
 50 55 60

Leu Arg Leu Glu Thr Ala Pro Asn Ile Ser Lys Asp Ala Ile Arg Gln
 65 70 75 80

Leu Leu Pro Arg Ala Pro Pro Leu Arg Glu Leu Ile Asp Gln Tyr Asp
 85 90 95

Substitute Sequence Listing 08702-0100.txt

Val Gln Arg Asp Asp Ser Ser Asp Gly Ser Leu Glu Asp Asp Asp Tyr
 100 105 110
 His Ala Thr Thr Glu Thr Ile Ile Thr Met Pro Thr Glu Ser Asp Phe
 115 120 125
 Leu Met Gln Ala Asp Gly Lys Pro Lys Cys Cys Phe Phe Lys Phe Ser
 130 135 140
 Ser Lys Ile Gln Tyr Asn Lys Val Val Lys Ala Gln Leu Trp Ile Tyr
 145 150 155 160
 Leu Arg Pro Val Lys Thr Pro Thr Thr Val Phe Val Gln Ile Leu Arg
 165 170 175
 Leu Ile Lys Pro Met Lys Asp Gly Thr Arg Tyr Thr Gly Ile Arg Ser
 180 185 190
 Leu Lys Leu Asp Met Ser Pro Gly Thr Gly Ile Trp Gln Ser Ile Asp
 195 200 205
 Val Lys Thr Val Leu Gln Asn Trp Leu Lys Gln Pro Glu Ser Asn Leu
 210 215 220
 Gly Ile Glu Ile Lys Ala Leu Asp Glu Asn Gly His Asp Leu Ala Val
 225 230 235 240
 Thr Phe Pro Gly Pro Gly Glu Asp Gly Leu Asn Pro Phe Leu Glu Val
 245 250 255
 Lys Val Thr Asp Thr Pro Lys Arg Ser Glu Pro Arg Gly Pro Thr Ile
 260 265 270
 Lys Pro Cys Pro Pro Cys Lys Cys Pro Ala Pro Asn Leu Glu Gly Gly
 275 280 285
 Pro Ser Val Phe Ile Phe Pro Pro Lys Ile Lys Asp Val Leu Met Ile
 290 295 300
 Ser Leu Ser Pro Ile Val Thr Cys Val Val Val Asp Val Ser Glu Asp
 305 310 315 320
 Asp Pro Asp Val Gln Ile Ser Trp Phe Val Asn Asn Val Glu Val His
 325 330 335
 Thr Ala Gln Thr Gln Thr His Arg Glu Asp Tyr Asn Ser Thr Leu Arg
 340 345 350

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Val Val Ser Ala Leu Pro Ile Gln His Gln Asp Trp Met Ser Gly Lys
 355 360 365

Ala Phe Ala Cys Ala Val Asn Asn Lys Asp Leu Pro Ala Pro Ile Glu
 370 375 380

Arg Thr Ile Ser Lys Pro Lys Gly Ser Val Arg Ala Pro Gln Val Tyr
 385 390 395 400

Val Leu Pro Pro Pro Glu Glu Glu Met Thr Lys Lys Gln Val Thr Leu
 405 410 415

Thr Cys Met Val Thr Asp Phe Met Pro Glu Asp Ile Tyr Val Glu Trp
 420 425 430

Thr Asn Asn Gly Lys Thr Glu Leu Asn Tyr Lys Asn Thr Glu Pro Val
 435 440 445

Leu Asp Ser Asp Gly Ser Tyr Phe Met Tyr Ser Lys Leu Arg Val Glu
 450 455 460

Lys Lys Asn Trp Val Glu Arg Asn Ser Tyr Ser Cys Ser Val Val His
 465 470 475 480

Glu Gly Leu His Asn His His Thr Thr Lys Ser Phe Ser Arg Thr Pro
 485 490 495

Gly Lys

<210> 21
 <211> 496
 <212> PRT
 <213> chimera

<400> 21

Met Met Gln Lys Leu Gln Phe Ile Tyr Val Tyr Ile Tyr Leu Phe Asn
 1 5 10 15

Leu Ile Ala Ala Gly Pro Val Asp Leu Asn Asn Ile Glu Gly Ser Glu
 20 25 30

Arg Glu Glu Asn Val Glu Lys Glu Gly Leu Cys Asn Ala Cys Ala Trp
 35 40 45

Arg Gln Asn Thr Arg Tyr Ser Arg Ile Glu Ala Ile Lys Ile Gln Ile
 50 55 60

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Leu Ser Lys Leu Arg Leu Glu Thr Ala Pro Ile Asn Ile Ser Lys Asp
 65 70 75 80
 Ala Ile Arg Gln Leu Leu Pro Arg Ala Pro Pro Leu Arg Glu Leu Ile
 85 90 95
 Asp Gln Tyr Asp Val Gln Arg Asp Asp Ser Ser Asp Gly Ser Leu Glu
 100 105 110
 Asp Asp Asp Tyr His Ala Thr Thr Glu Thr Ile Ile Thr Met Pro Thr
 115 120 125
 Glu Ser Asp Phe Leu Met Gln Ala Asp Gly Lys Pro Lys Cys Cys Phe
 130 135 140
 Phe Lys Phe Ser Ser Lys Ile Gln Tyr Asn Asn Asn Lys Val Val Lys
 145 150 155 160
 Ala Gln Leu Trp Ile Tyr Leu Arg Pro Val Lys Thr Pro Thr Thr Val
 165 170 175
 Phe Val Gln Ile Leu Arg Leu Ile Lys Pro Met Lys Asp Gly Thr Arg
 180 185 190
 Tyr Thr Gly Ile Arg Ser Leu Lys Leu Asp Met Ser Pro Gly Thr Gly
 195 200 205
 Ile Trp Gln Ser Ile Asp Val Lys Thr Val Leu Gln Asn Trp Leu Lys
 210 215 220
 Gln Pro Glu Ser Asn Leu Gly Ile Glu Ile Lys Ala Leu Asp Glu Asn
 225 230 235 240
 Gly His Asp Leu Ala Val Thr Phe Pro Gly Pro Gly Glu Asp Gly Leu
 245 250 255
 Asn Pro Phe Leu Glu Val Lys Val Thr Asp Thr Pro Lys Arg Ser Gly
 260 265 270
 Ser Gly Ser Glu Pro Arg Gly Pro Thr Ile Lys Pro Cys Pro Pro Cys
 275 280 285
 Lys Cys Pro Ala Pro Asn Leu Glu Gly Gly Pro Ser Val Phe Ile Phe
 290 295 300
 Pro Pro Lys Ile Lys Asp Val Leu Met Ile Ser Leu Ser Pro Ile Val

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305 310 315 320

Thr Cys Val Val Val Asp Val Ser Glu Asp Asp Pro Asp Val Gln Ile
325 330 335

Ser Val His Thr Ala Gln Thr Gln Thr His Arg Glu Asp Tyr Asn Ser
340 345 350

Thr Leu Arg Val Val Ser Ala Leu Pro Ile Gln His Gln Asp Trp Met
355 360 365

Ser Gly Lys Ala Phe Ala Cys Ala Val Asn Asn Lys Asp Leu Pro Ala
370 375 380

Pro Ile Glu Arg Thr Ile Ser Lys Pro Lys Gly Ser Val Arg Ala Pro
385 390 395 400

Gln Val Tyr Val Leu Pro Pro Pro Glu Glu Glu Met Thr Lys Lys Gln
405 410 415

Val Thr Leu Thr Cys Met Val Thr Asp Phe Met Pro Glu Asp Ile Tyr
420 425 430

Val Glu Trp Thr Asn Asn Gly Lys Thr Glu Leu Asn Tyr Lys Asn Thr
435 440 445

Glu Pro Val Leu Asp Ser Asp Gly Ser Tyr Phe Met Tyr Ser Lys Leu
450 455 460

Arg Val Glu Lys Arg Asn Ser Tyr Ser Cys Ser Val Val His Glu Gly
465 470 475 480

Leu His Asn His His Thr Thr Lys Ser Phe Ser Arg Thr Pro Gly Lys
485 490 495

<210> 22
<211> 497
<212> PRT
<213> chimera

<400> 22

Met Met Gln Lys Leu Gln Leu Cys Val Tyr Ile Tyr Leu Phe Met Leu
1 5 10 15

Ile Val Ala Gly Pro Val Asp Leu Asn Glu Asn Ser Glu Gln Lys Glu
20 25 30

Asn Val Glu Lys Glu Gly Leu Cys Asn Ala Cys Thr Trp Arg Gln Asn
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35

40

45

Thr Lys Ser Ser Arg Ile Glu Ala Ile Lys Ile Gln Ile Leu Ser Lys
50 55 60

Leu Arg Leu Glu Thr Ala Pro Asn Ile Ser Lys Asp Val Ile Arg Gln
65 70 75 80

Leu Leu Pro Lys Ala Pro Pro Leu Arg Glu Leu Ile Asp Gln Tyr Asp
85 90 95

Val Gln Arg Asp Asp Ser Ser Asp Gly Ser Leu Glu Asp Asp Asp Tyr
100 105 110

His Ala Thr Thr Glu Thr Ile Ile Thr Met Pro Thr Glu Ser Asp Phe
115 120 125

Leu Met Gln Val Asp Gly Lys Pro Lys Cys Cys Phe Phe Lys Phe Ser
130 135 140

Ser Lys Ile Gln Tyr Asn Lys Val Val Lys Ala Gln Leu Trp Ile Tyr
145 150 155 160

Leu Arg Pro Val Glu Thr Pro Thr Thr Val Phe Val Gln Ile Leu Arg
165 170 175

Leu Ile Lys Pro Met Lys Asp Gly Thr Arg Tyr Thr Gly Ile Arg Ser
180 185 190

Leu Lys Leu Asp Met Asn Pro Gly Thr Gly Ile Trp Gln Ser Ile Asp
195 200 205

Val Lys Thr Val Leu Gln Asn Trp Leu Lys Gln Pro Glu Ser Asn Leu
210 215 220

Gly Ile Glu Ile Lys Ala Leu Asp Glu Asn Gly His Asp Leu Ala Val
225 230 235 240

Thr Phe Pro Gly Pro Gly Glu Asp Gly Leu Asn Pro Phe Leu Glu Val
245 250 255

Lys Val Thr Asp Thr Pro Lys Arg Ser Glu Pro Lys Ser Cys Asp Lys
260 265 270

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro
275 280 285

Substitute Sequence Listing 08702-0100.txt

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser
290 295 300

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp
305 310 315 320

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn
325 330 335

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val
340 345 350

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu
355 360 365

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys
370 375 380

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr
385 390 395 400

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr
405 410 415

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu
420 425 430

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu
435 440 445

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys
450 455 460

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu
465 470 475 480

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
485 490 495

Lys

<210> 23
<211> 491
<212> PRT
<213> chimera

<400> 23

Substitute Sequence Listing 08702-0100.txt

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Met Gln Lys Leu Gln Leu Cys Val Tyr Ile Tyr Leu Phe Met Leu Ile
1      5      10      15

Val Ala Gly Pro Val Asp Leu Asn Glu Asn Ser Glu Gln Lys Glu Asn
      20      25      30

Val Glu Lys Glu Gly Leu Cys Asn Ala Cys Thr Trp Arg Gln Asn Thr
      35      40      45

Lys Ser Ser Arg Ile Glu Ala Ile Lys Ile Gln Ile Leu Ser Lys Leu
      50      55      60

Arg Leu Glu Thr Ala Pro Asn Ile Ser Lys Asp Val Ile Arg Gln Leu
      65      70      75      80

Leu Pro Lys Ala Pro Pro Leu Arg Glu Leu Ile Asp Gln Tyr Asp Val
      85      90      95

Gln Arg Asp Asp Ser Ser Asp Gly Ser Leu Glu Asp Asp Asp Tyr His
      100      105      110

Ala Thr Thr Glu Thr Ile Ile Thr Met Pro Thr Glu Ser Asp Phe Leu
      115      120      125

Met Gln Val Asp Gly Lys Pro Lys Cys Cys Phe Phe Lys Phe Ser Ser
      130      135      140

Lys Ile Gln Tyr Asn Lys Val Val Lys Ala Gln Leu Trp Ile Tyr Leu
      145      150      155      160

Arg Pro Val Glu Thr Pro Thr Thr Val Phe Val Gln Ile Leu Arg Leu
      165      170      175

Ile Lys Pro Met Lys Asp Gly Thr Arg Tyr Thr Gly Ile Arg Ser Leu
      180      185      190

Lys Leu Asp Met Asn Pro Gly Thr Gly Ile Trp Gln Ser Ile Asp Val
      195      200      205

Lys Thr Val Leu Gln Asn Trp Leu Lys Gln Pro Glu Ser Asn Leu Gly
      210      215      220

Ile Glu Ile Lys Ala Leu Asp Glu Asn Gly His Asp Leu Ala Val Thr
      225      230      235      240

Phe Pro Gly Pro Gly Glu Asp Gly Leu Asn Pro Phe Leu Glu Val Lys
      245      250      255

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Val Thr Asp Thr Pro Lys Arg Ser Asp Lys Thr His Thr Cys Pro Pro
260 265 270

Cys Pro Ala Pro Glu Ala Leu Gly Ala Pro Ser Val Phe Leu Phe Pro
275 280 285

Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr
290 295 300

Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn
305 310 315 320

Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
325 330 335

Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
340 345 350

Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
355 360 365

Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys
370 375 380

Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu
385 390 395 400

Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
405 410 415

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
420 425 430

Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe
435 440 445

Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
450 455 460

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
465 470 475 480

Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
485 490

Substitute Sequence Listing 08702-0100.txt